'New' human adenovirus may not make for good vaccines, after all

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In recent years, scientists have studied the possibility of using engineered human adenoviruses as vaccines against diseases such as HIV, tuberculosis, and malaria. In this approach, adenoviruses, which commonly cause respiratory-tract infections, are rendered relatively harmless before they are used as vectors to deliver genes from pathogens, which in turn stimulate the body to generate a protective immune response.

In a new study of four adenovirus vectors, researchers from The Wistar Institute show that a reportedly rare human adenovirus, called AdHu26, is not so rare, after all, and would thus be unlikely to be optimal as a vaccine carrier for mass vaccination. As previous research has shown, a viral vector may be ineffective if the virus it is based on is common in a given population. According to the Wistar scientists, their study also supports the use of chimpanzee adenoviruses as vaccine vectors, since humans have little exposure to these viruses. Their findings were published online, ahead of print, in the *Journal of Virology*.

"Despite previous reports to the contrary, we find that AdHu26 commonly infects people, particularly those in Sub-Saharan Africa, the very people for whom the need for novel vaccine strategies is most dire," said senior author Hildegund C. J. Ertl, M.D., Wistar professor and director of The Wistar Institute's Vaccine Center. "HIV, malaria, and other infectious diseases take a tremendous toll in the developing world, especially in Sub-Saharan Africa, and a vaccine platform that could be used in those regions could save the lives of millions."

Scientists believe that prior immunity to human adenoviruses is what led, in part, to the failure in 2007 of the STEP trial, a large vaccine trial in the US and other countries that used an adenovirus vector as the basis for an HIV vaccine.

In the current study, Ertl and her colleagues analyzed blood samples collected from people at seven sites around the world, including Thailand, the United States, and five sub-Saharan African nations. They tested the samples to see if they contained neutralizing antibodies and responsive immune cells when exposed to AdHu26 and AdHu5, the virus used in the STEP trial. Surprisingly, neutralizing antibodies to AdHu26 were very prevalent in blood.

According to Ertl, adenoviruses are still good vaccine vectors, just not necessarily human adenoviruses.

In addition to testing AdHu5 and AdHu26, the Wistar scientists also tested two adenoviruses that originated in chimpanzees, called AdC6 and AdC7. As expected, neutralizing antibodies were far less likely to be detected in human samples. Mouse studies of all four vectors demonstrated that that were similar in their ability to generate cellular immune responses.

"This study also confirms our current line of research that suggests engineered chimpanzee adenovirus vectors could be superior to related, native human adenoviruses," Ertl said. "Both human and chimpanzee adenoviruses function in similar ways, but the simple benefit is that humans are rarely exposed to adenoviruses of chimpanzee origin."

The Ertl laboratory is currently developing an HIV vaccine utilizing chimpanzee adenoviruses.

Provided by The Wistar Institute